09/807122
JC07 Rec'd PCT/PTO 06 APR 2001

Atty. Docket #: 198at29

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

INTERNATIONAL APPL. NO.: PCT/EP99/07084 :		
INTERNATIONAL FILING DATE: -09/23/1999- :		
APPLICANT: KARL-JOSEF HAACK ET AL :		
SERIAL NO:	:	**ART UNIT:**
FILED: -HEREWITH-	:	**EXAMINER:**
FOR: "SUBSTITUTED ISOPHOSPHINDOLINES AND THEIR USE" :		

Commissioner for Patents
Box PCT
Washington, D.C. 20231

"Express Mail" No.: EE617838404 **Date:** - APRIL 06, 2001 -

I hereby certify that this paper, along with any other paper or fee referred to in this paper as being transmitted herewith, is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10, postage prepaid, on the date indicated above, addressed to the Commissioner for Patents, Washington, D.C. 20231

-Carrie A. McPherson-
(Typed or printed name of mailing paper or fee)

(Signature of person mailing paper)

TRANSMITTAL OF APPLICATION PAPERS TO U.S. DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. §371 (37 CFR 1.494 OR 1.495)

This Transmittal Letter is based upon PTO Form 1390 (as revised in May, 1993).

The above-identified applicant(s) (jointly with their assignee) have filed an International Application under the P.C.T. and hereby submit(s) to the United States Designated/Elected Office (DO/EO/US) the following items and other information.

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1. [X] This is a FIRST submission of items concerning a filing under 35 U.S.C. §371.

2. [ ] This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. §371.

3. [X] This is an express request to begin national examination procedures (35 U.S.C. §371[f]) at any time rather than delay.

4. [ ] A proper Demand for International Preliminary Examination (IPE) was made to the appropriate Authority (IPEA) within the time period required.

5. [X] A copy of the International Application as filed (35 U.S.C. §371[c][2]) --
   a. [X] is transmitted herewith (required when not transmitted by International Bureau).
   b. [ ] has been transmitted by the International Bureau. See WIPO Publication WO 00/21971.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).

6. [X] A (verified) translation of the International Application into the English language is enclosed.

7. [ ] Amendments to the (specification and) claims of the International Application under PCT Article 19 (35 U.S.C. 371[c][3])
   a. [ ] are transmitted herewith (required if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
   e. [ ] will be submitted with the appropriate surcharge.

8. [ ] A translation of the amendments to the claims (and/or the specification) under PCT Article 19 (35 U.S.C. §371[c][3]) is enclosed or will be submitted with the appropriate surcharge.

9. [X] An oath or declaration/power of attorney of the inventor(s) (35 U.S.C. §371[c][4]) will follow.
   [ ] and is attached to the translation of (or a copy of) the International Application.
   [ ] and is attached to the substitute specification.

10. [ ] A translation of at least the Annexes to the IPE Report under PCT Article 36 (35 U.S.C. §371[c][5]) is enclosed.

Items 11. to 16. below concern other document(s) or information included:

11. [X] An Information Disclosure Statement under 37 CFR 1.97 and 1.98 is enclosed.

12. [X] An Assignment for recording and a separate cover sheet in compliance with 37 CFR 3.28 and 3.31 will follow.

13. [X] A FIRST preliminary amendment is enclosed.
    A SECOND or SUBSEQUENT preliminary amendment is enclosed.

14. [ ] A substitute specification (including claims, abstract, drawing) is enclosed.

15. [ ] A change of power of attorney and/or address letter is enclosed.

16. [X] Other items of information:

    [X] This application is being filed pursuant to 37 CFR 1.494(c) or 1.495(c), and any missing parts will be filed before expiration of--

        [ ] 22 months from the priority date under 37 CFR 1.494(c), or

        [X] 32 months from the priority date under 37 CFR 1.495(c).

    [X] The undersigned attorney is authorized by the International applicant and by the inventors to enter the National Phase pursuant to 37 CFR 1.494(c) or 1.495(c).

The following additional information relates to the International Application:

[X] Receiving Office: EPO
[X] IPEA (if filing under 37 CFR 1.495): EPO
[X] Priority Claim(s) (35 USC §§ 119, 365):
German Appln. 198 46 559.9 filed -October 09, 1998-.
[X] A copy of the International Search Report is

[ ] enclosed.
[X] attached to the copy of the International Application.

[X] A copy of the Receiving Office Request Form is enclosed.

[X] Form PTO/SB/05 - 1 sheet
[X] Form PCT/IB/308 - 2 sheets
[X] AMENDED SHEETS (spec) pp. 3,4,5,7,8 & 9 IN
(claims)pp. 16, 17 & 18 [1-15] ENGLISH
[X] AMENDED SHEETS (spec) pp. 4,5,8,9 IN GERMAN
(claism)pp. 17, 18 & 19 [1-15]

The fee calculation is set forth on the next page of this Transmittal Letter.

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FEE CALCULATION SHEET

[x] A check in payment of the filing fee, calculated as follows, is attached (37 CFR 1.492).

Basic Fee.....	$ 860.00
Total Number of claims in excess of (20) times $18.....	-0-
Number of independent claims in excess of (3) times $80.....	-0-
Fee for multiple dependent claims $270.....	-0-
TOTAL FILING FEE...	$ 860.00

Kindly send us the official filing receipt.

The Commissioner is hereby authorized to charge any additional fees which may be required or to credit any overpayment to Deposit Account No. 03-2775. This is a "general authorization" under 37 CFR 1.25(b), except that no automatic debit of the issue upon allowance is authorized. An additional copy of this page is attached.

Respectfully submitted,

By _____

Ashley I. Pezzner
Reg. No. 35,646
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1220 Market Street
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Tel. (302) 658-9141

AIP/cam (8602*32)
Enclosures
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09/807122
JC08 Rec'd PCT/PTO 06 APR 2001

198at29 (8602*32)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: KARL-JOSEF HAACK *ET AL.*	)
	)
SERIAL NO. TO BE ASSIGNED	) **ART UNIT: TO BE ASSIGNED**
	)
FILED: HEREWITH	) **EXAMINER: TO BE ASSIGNED**
	)
FOR: SUBSTITUTED ISOPHOSPHINDOLINES AND THEIR USE	)
	)

Asst. Commissioner for Patents
Washington, D.C. 20231

"EXPRESS MAIL" NO. EE617838404 DATE: APRIL 6, 2001

I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE "EXPRESS MAIL POST OFFICE TO ADDRESSEE" SERVICE UNDER 37 CFR 1.10 ON THE DATE INDICATED AND IS ADDRESSED TO THE ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231

CARRIE A. MCPHERSON
(TYPED OR PRINTED NAME OF PERSON MAILING PAPER OR FEE)

Carrie A. McPherson
(SIGNATURE OF PERSON MAILING PAPER OR FEE)

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PRELIMINARY AMENDMENT

Sir:

Prior to fee calculation and examination please amend the above-identified application as follows.

In the Claims

Please cancel claims 1-16.

Please add the following new claim(s).

--17. A complex of the formula (XIV)

$$[M_xP_mL_nS_q]Y_r \qquad \text{(XIV)}$$

wherein

M is a metal center,

P are organic ligands,

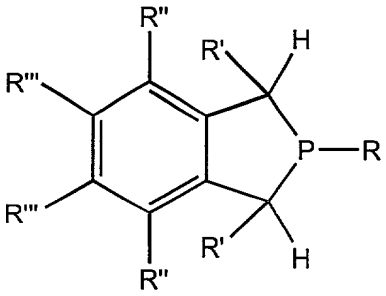
L are identical or different organic or inorganic ligands,

S are coordinating solvent molecules and

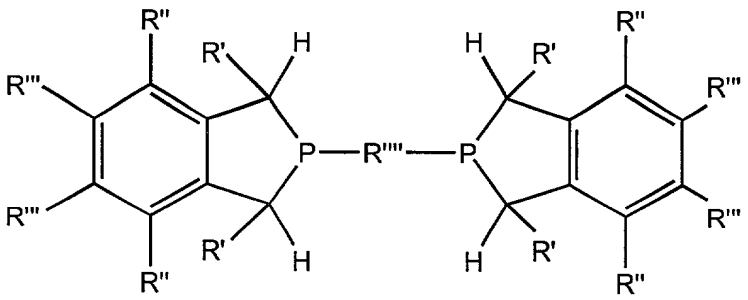
Y are noncoordinating anionic equivalents

and x and m are integers greater than or equal to 1,

n, q and r are integers greater than or equal to 0, in which one or more identical or different isophosphindolines of the type (VII) or (XIII)



(VII)



(XIII)

wherein

R is hydrogen or an alkyl, aryl, haloaryl or haloalkyl group,

R' are alkyl, aryl, haloaryl or haloalkyl groups,

R" and R''' are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl, haloaryl, alkoxy, amino, dialkylamino, sulfonate groups or fluorine and two adjacent radicals R"/R", R"/R''' or R'''/R''' are optionally bridged, and

R'''' is an alkanediyl, arenediyl or heteroarenediyl group, wherein the term alkyl or haloalkyl group encompasses the corresponding cyclo compounds,

are present as ligands P.

18. The complex as claimed in claim 17, wherein the sum m + n + q is less than or equal to 6x.

19. The complex as claimed in claim 17, wherein x is less than 4.

20. The complex as claimed in claim 17, wherein the metal center or centers M_x comprise at least one transition metal.

21. The complex as claimed in claim 20, wherein the alkyl, aryl, haloalkyl, haloaryl, alkoxy or dialkylamino group each have, independently of one another, having from 1 to 20 carbon atoms.

22. The complex as claimed in claim 17, wherein the haloalkyl group is CF_3, CH_2CF_3 or C_2F_5.

23. The complex as claimed in claim 17, wherein said R"" has from 2 to 20 carbon atoms.

24. The complex as claimed in claim 17, wherein said R"" is ethane-1,2-diyl, benzene-1,2-diyl or furan-3,4-diyl.

25. The complex as claimed in claim 17, wherein R is phenyl, R' is methyl or ethyl, R" and R"' are identical or different and are hydrogen, methyl or phenylene, R"" is benzene-1,2-diyl.

26. The complex as claimed in claim 17, wherein said P is chiral liagnd.

27. The complex as claimed in claim 17, wherein said P is an isophosphindoline of the formula (VII) which has two asymmetric centers having the same absolute configuration in positions 1 and 3.

28. The complex as claimed in claim 17, wherein P is an isophosphindoline of the formula (XIII) which has three or four asymmetric centers having the same absolute configuration in positions, 1, 1', 3 and 3'.

29. The complex as claimed in claim 17, wherein R is phenyl, R' is methyl, R" and R'" are hydrogen and R"" is benzene-1,2-diyl.

30. The complex as claimed in claim 17, which is enriched in one enantiomer.

31. A catalyst which is useful in asymmetric reactions, polymerization reactions, transfer hydrogenations, rearrangements, cyclopropanations, or Heck reactions which comprises the complex as claimed in claim 17.

32. The complex as claimed in claim 20, wherein M is palladium, platinum, rhodium, ruthenium, osmium, iridium, cobalt, nickel or copper.

33. The complex as claimed in claim 21, wherein the alkyl, aryl, haloalkyl, haloaryl, alkoxy or dialkylamino group each have, independently of one another, from 1 to 6 carbon atoms.

34. The complex as claimed in claim 23, wherein said R"" has from 2, 3, 4, 5 or 6 carbon atoms.

35. The complex as claimed in claim 23, wherein the R"" has from 2 or 6 carbon atoms.

36. In a process for asymmetric reactions wherein the improvement comprises using the catalyst as claimed in claim 31.--

REMARKS

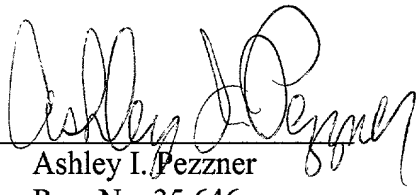
The applicants respectfully request that the preliminary amendment be entered prior to fee calculation and examination. Support for newly added claims 17-36 can be found in the original claims 1-16. No additional fee is due. If there are any additional fees due in connection with the filing of this response, the Commissioner is authorized to charge or credit any overpayment to

Deposit Account No. 03-2775.

A prompt and favorable action is solicited.

Respectfully submitted,

CONNOLLY BOVE LODGE & HUTZ LLP

By 

Ashley I. Pezzner
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AIP/cam
::ODMA\MHODMA\CB;138121;1

Filed 12/29/2005

Substituted isophosphindolines and their use

Description

The invention relates to substituted isophosphindolines and their metal complexes.

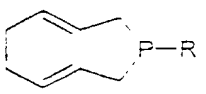
Phosphorus compounds, in particular trisubstituted phosphines, have great importance as ligands in homogeneous catalysis. Variation of the substituents on the phosphorus in such phosphorus compounds enables the electronic and stearic properties of the phosphorus ligand to be influenced in a targeted way, so that selectivity and activity in homogeneously catalyzed processes can be controlled.

The variety of structures of phosphorus ligands known hitherto is very great. These ligands can, for example, be classified by class of compound, and examples of such classes of compounds are trialkylphosphines and triarylphosphines, phosphites, phosphonites, etc. This classification according to classes of compounds is particularly useful for describing the electronic properties of the ligands.
Classification of phosphorus ligands according to their symmetry properties or according to the number of coordination positions occupied by the ligands is also possible. This structuring takes account of, in particular, the stability, activity and (potential) stereoselectivity of metal complexes bearing phosphorus ligands as catalyst precursors/catalysts.

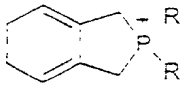
Enantiomerically enriched chiral ligands are used in asymmetric synthesis or asymmetric catalysis; an important aspect here is that the electronic *and* the stereochemical properties of the ligand are optimally matched to the respective catalysis problem. There is a great need for chiral ligands which differ stereochemically or/and electronically in order to find the optimum "tailored" ligands for a particular asymmetric catalysis. In the ideal case, therefore, one has available a flexibly modifiable, chiral ligand skeleton whose stearic and electronic properties can be varied within a wide range. Examples of such a basic ligand skeleton are metallocene catalysts for stereoselective olefin polymerization or for asymmetric catalysis.

Within the class of cyclic phosphines, the phospholines have achieved particular importance. Examples of bidentate, chiral phospholines are the DuPhos and BPE ligands used in asymmetric catalysis (Burk et al., Specialty Chemicals, 1998, 58). Although these can be varied stearically within a relatively broad range, they can be varied electronically to only a very limited extent, i.e. by replacement of the arenediyl backbone in the DuPhos ligands by an ethane-1,2-diyl backbone in the BPE ligands.

The class of isophosphindolines of the formula (I) is quite similar to that of the phospholines, but is known from the literature in the form of only a few representatives: thus, known compounds are, for example the parent compound isophosphindoline of the formula (Ia) (Robinson et al., J. Heterocycl. Chem., 1973, 395) and alkyl or aryl derivatives of isophosphindoline of the formula (Ib, Ic) (Mann et al., J. Chem. Soc., 1954, 2832; Schmidbaur et al., J. Organomet. Chem. 250, 1983, 171; Breen et al., J. Am. Chem. Soc., 1995, 11914), also phosphonium salts of the isophosphindoline of the formula (II) (Mann et al., J. Chem. Soc., 1954, 2832; ibid. 1958, 2516; Schmidbaur et al., J. Organomet. Chem. 250, 1983, 171).



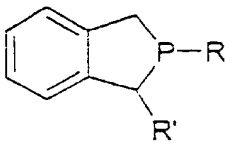
(I)



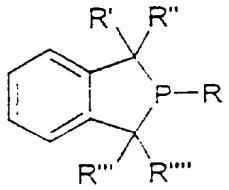
(II)

In formula (Ia), R is hydrogen, while in the formulae (Ib/c) and (II), R is an alkyl or aryl radical.

Representatives which are substituted on the aliphatic carbon skeleton of the isophosphindoline are likewise known, but the compounds known hitherto are either monosubstituted derivatives of the formula (III) (Fluck et al., Phosphorous Sulfur, 1987, 121; Quin et al., J. Org. Chem., 1986, 3235) or derivatives of the formula (IV) which are mentioned in WO 96/16100 and WO 96/23829 but have obviously not been synthesized hitherto.

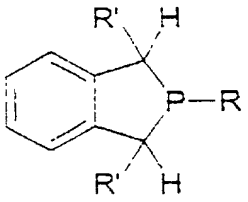


(III)

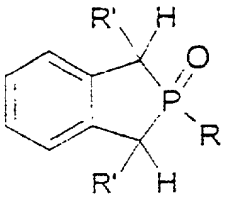


(IV)

1,3-Disubstituted isophosphindolines (V) have previously only been known in the form of their phosphine oxides (VIa, VIb) (Holland et al., J. Chem. Soc. Perkin Trans. 1, 1973, 927):



(V)



R' = Ph, R = Me: **(VIa)**
R' = Ph, R = Ph: **(VIb)**

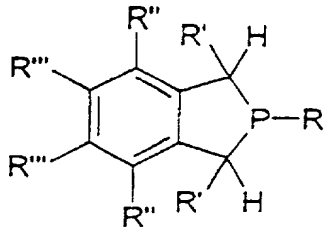
(VI)

The 1,3-disubstituted isophosphindolines of the formula (V), which have not been described hitherto, are achiral if the two asymmetric centers on C1 and C3 have different (opposite) absolute configurations (meso form). The remaining representatives are chiral (c_2 symmetry). The chiral representatives are of particular importance since they can be used as ligands in asymmetric, catalytic syntheses.

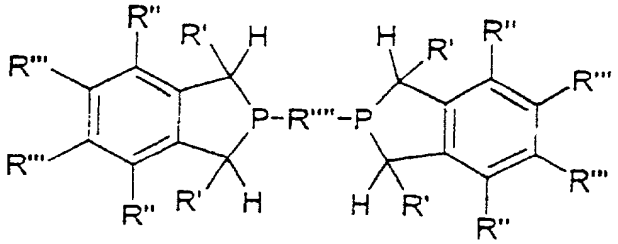
Like the substances of the formula (V), their derivatives substituted on the aromatic carbon skeleton have also not been described hitherto.

The previously known and used phospholine ligands DuPhos and BPE have, as mentioned above, the disadvantage that their electronic properties can be varied to only a very small extent. It is therefore an object of the present invention to provide a basic ligand skeleton which can be varied in a manner analogous to the previously known phospholine ligands but also be varied electronically within a wide range.

This object is achieved by the provision of substituted isophosphindolines of the formula (VII) or (XIII),



(VII)



(XIII)

where, in the formula (VII),

R	is hydrogen or an alkyl, aryl, haloaryl or haloalkyl group,
R'	are alkyl, aryl, haloaryl or haloalkyl groups,
R" and R"'	are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl or haloaryl, alkoxy, amino, dialkylamino or sulfonate groups or fluorine and two adjacent radicals R"/R", R"/R"' or R"'/R"' may also be bridged,

and, in the formula (XIII)

R'	are alkyl, aryl, haloaryl or haloalkyl groups,
R" and R"'	are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl or haloaryl, alkoxy, amino, dialkylamino or sulfonate groups or fluorine and two adjacent radicals R"/R", R"/R"' or R"'/R"' may also be bridged, and
R""	is an alkanediyl, arenediyl or heteroarenediyl group.

For the present purposes, alkyl and haloalkyl groups include the corresponding cyclo compounds. Particular preference is given to chiral substituted isophosphindolines.

The substituted isophosphindoline of the invention preferably bears alkyl, aryl, haloaryl, haloalkyl, alkoxy or/and dialkylamino groups which are

SUBSTITUTE SHEET (RULE 26)

selected independently of one another and each contain from 1 to 20, in particular from 1 to 6, carbon atoms.

The haloalkyl or/and haloaryl groups preferably have the formulae $CHal_3$, CH_2CHal_3, C_2Hal_5, where Hal can be, in particular, F, Cl or Br. Particular preference is given to haloalkyl or/and haloaryl groups of the formulae CF_3, CH_2CF_3, C_2F_5.

It is also preferred that the alkanediyl, arenediyl or heteroarenediyl group R"" of the substituted isophosphindoline has from 2 to 20 carbon atoms, more preferably 2, 3, 4, 5 or 6 carbon atoms, in particular 2 or 6 carbon atoms. Ethane-1,2-diyl, benzene-1,2-diyl or furan-3,4-diyl are particularly preferred examples of alkanediyl, arenediyl or heteroarenediyl groups R"".

Furthermore, preference is given to a substituted isophosphindoline in which R is phenyl, R' is methyl or ethyl, R" and R"' is hydrogen, methyl or/and phenylene, R"" is benzene-1,2-diyl. Particular preference is given to a substituted isophosphindoline in which R is phenyl, R' is methyl or ethyl, R" and R"' are hydrogen, methyl or/and phenylene, R"" is benzene-1,2-diyl, in which R" and R"' are not hydrogen or in which either R" or R"' is hydrogen.

Furthermore, preference is given to substituted isophosphindolines whose asymmetric centers in the 1 and 3 positions have the same absolute configuration. The substituted isophosphindoline of the formula (VII) has two asymmetric centers having the same absolute configuration in positions 1 and 3, while in the case of those of the formula (XIII), each has two or four asymmetric centers having the same absolute configuration in the positions 1, 1', 3 and 3'.

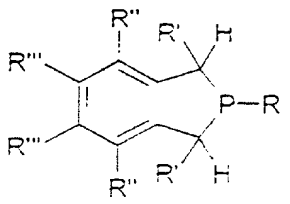
Finally, preference is given to substituted chiral isophosphindolines which are enriched in one enantiomer.

The substituents R' in the substances of the formulae (VII) and (XIII) are essential for the *steric* properties of the ligands, while the other substituents R, R", R"' and R"" essentially determine the *electronic* properties by means of their donor or acceptor capabilities, and thus allow, as explained above,

the reactivity, selectivity and application range in respect of substrates in catalytic reactions to be influenced over a wide range.

A further substantial difference between the compounds of the formulae (VII) and (XIII) on the one hand and phospholines on the other hand is the greater rigidity of the five-membered heterocyclic ring in the compounds of the formulae (VII) and (XIII), which in attributable to the replacement of the ethanediyl backbone in the phospholines by the benzene-1,2-diyl substituent in the substances of the formulae (VII) and (XIII).

Representatives of the class of compounds of the formula (VII), which encompasses not only compounds of the formula (V) but also corresponding compounds substituted in the fused-on aromatic ring, have been prepared. In cases where these are chiral, the compounds have also been synthesized in a form enriched in one enantiomer.



(VII)

A number of routes are available for the synthesis of the substituted isophosphindolines of the formula (VII): for example, either the corresponding phthalic dialdehyde of the formula (VIII) or the corresponding diketone of the formula (IX) can be used as starting material.

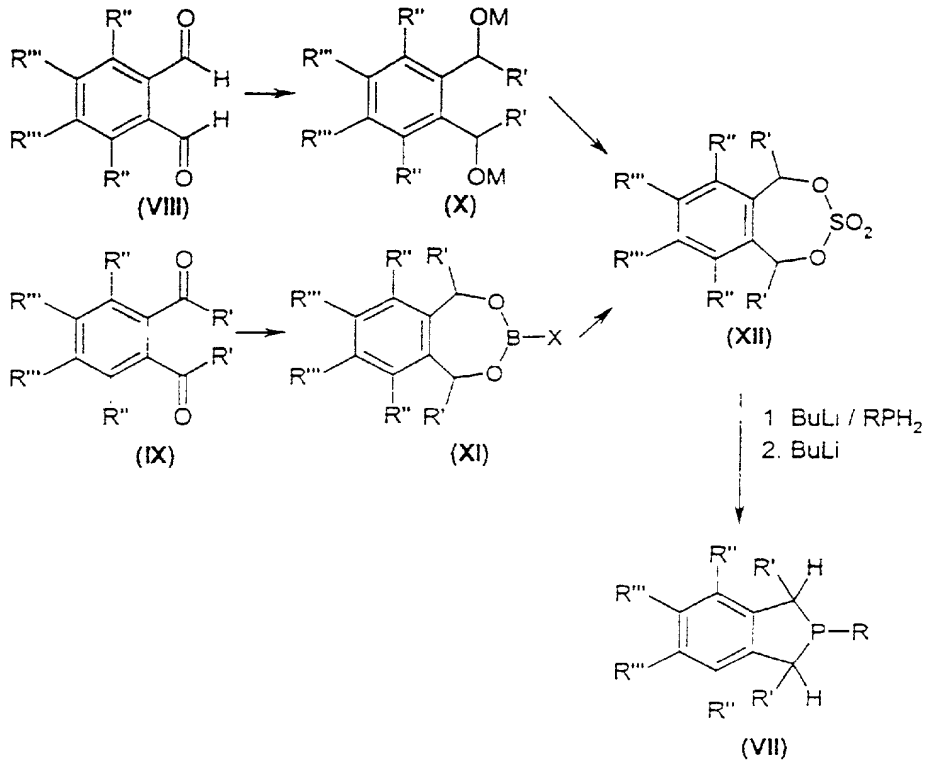
The reaction of the phthalic dialdehyde of the formula (VIII) with two equivalents of Grignard R'-M gives firstly the corresponding dialkoxide of the formula (X) which can be reacted further to give the cyclic sulfate of the formula (XII).

Starting from the diketone of the formula (IX), this is firstly reduced by means of boron compounds or analogous compounds to give the boronic

acid derivative (XI) which can likewise be converted into the cyclic sulfate (XII).

A single representative of the sulfates of the formula (XII) is a previously known compound in which R' = methyl and R" = R"' = H and which is mentioned in WO 97/13763, page 7.

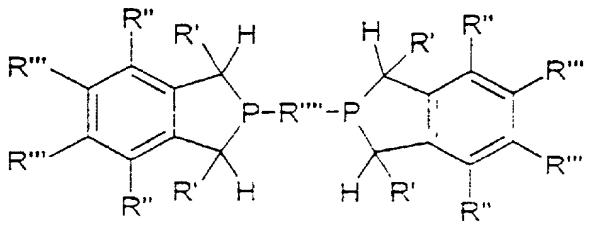
Depending on reaction conditions, synthetic route and reagent, the sulfate of the formula (XII) is obtained as a mixture of diastereomers (meso/rac form) or/and enantiomers; separation of the isomers gives the stereochemically pure sulfate of the formula (XII).



In a modification of known processes (Burk US 5,386,061), reaction of the sulfate of the formula (XII) with phosphines of the formula RPH_2 (R = alkyl, aryl, heteroaryl) gives, via the corresponding phosphides, the corresponding substituted isophosphindoline.

It is likewise possible to convert the isomer mixture of the sulfate of the formula (XII) into the corresponding mixture of isomeric isophosphindolines and then to carry out a separation in order to obtain stereochemically pure substituted isophosphindolines. This separation can be achieved, for example, by fractional crystallization and/or chromatographically.

As phosphines of the formula RPH_2, it is possible to use all types of arylphosphines and alkylphosphines as starting materials (R = aryl, alkyl). If, instead of these, diphosphines of the formula $H_2P=R''''-PH_2$ are used, the products are chelating ligands of the formula (XIII) which in the case of c_2-symmetric sulfates of the formula (XII) lead to chiral and then likewise c_2-symmetric chelating ligands.



(XIII)

The compounds of the formulae (VII) and (XIII) can be used as ligands on metals in asymmetric, metal-catalyzed reactions (e.g. asymmetric hydrogenation, asymmetric rearrangement, asymmetric cyclopropanation or Heck reactions) and in polymerizations. They are particularly useful for asymmetric reactions.

The ligands of the formulae (VII) and (XIII) form complexes of the type (XIV),

$$[M_xP_mL_nS_q]Y_r \qquad (XIV)$$

where, in the formula (XIV), M is a metal center, preferably a transition metal center, L are identical or different coordinating organic or inorganic ligands and P are organic ligands, according to the invention isophosphindolines of the type (VII) or (XIII), S are coordinating solvent molecules and Y are equivalents of noncoordinating anions, where x and m

are integers greater than or equal to 1, n, q and r are integers greater than or equal to 0.

The maximum value of the sum m + n + q is determined by the number of coordination sites available on the metal centers, but not all coordination sites have to be occupied. Preference is given to complexes having an octahedral, pseudo octahedral, tetrahedral, pseudo tetrahedral or square planar coordination sphere, which may also be distorted, around the respective transition metal center. In such complexes, the sum m + n + q is smaller than or equal to 6x.

The complexes of the present invention contain at least one metal atom or ion, preferably a transition metal atom or ion, in particular one selected from the group consisting of palladium, platinum, rhodium, ruthenium, osmium, iridium, cobalt, nickel and copper.

Preference is given to complexes having less than four metal centers, particularly preferably ones having one or more two metal centers. The metal centers can be occupied by various metal atoms and ions.

Preferred ligands L in such complexes are halide, particularly Cl, Br and I, diene, particularly cyclooctadiene, norbornadiene, olefin, particularly ethylene and cyclooctene, acetato, trifluoroacetato, acetylacetonato, allyl, methylallyl, alkyl, particularly methyl and ethyl, nitrile, particularly acetonitrile and benzonitrile, and also carbonyl and hydrido ligands.

Preferred coordinating solvents S are amines, particularly triethylamine, alcohols, particularly methanol, and aromatics, particularly benzene and cumene.

Preferred noncoordinating anions Y are trifluoroacetate, BF_4, ClO_4, PF_6 and BAr_4.

In the individual complexes, different molecules, atoms or ions of the individual constituents M, P, L, S and Y may be present.

Among the ionic complexes, preference is given to compounds of the type $[RhP_m(diene)]^+Y^-$, where P_m represents either two isophosphindolines of the type (VII) or one isophosphindoline of the type (XIII).

These metal-ligand complexes can be prepared in situ by reaction of a metal salt or an appropriate precursor complex with the ligands of the formulae (VII) and (XIII). Alternatively, a metal-ligand complex can be obtained by reaction of a metal salt or an appropriate precursor complex with the ligands of the formula (VII) and (XIII) and subsequent isolation.

Examples of metal salts are metal chlorides, bromides, iodides, cyanides, nitrates, acetates, acetylacetonates, hexafluoroacetylacetonates, perfluoroacetates or triflates, in particular of palladium, platinum, rhodium, ruthenium, osmium, iridium, cobalt, nickel and/or copper.

Examples of precursor complexes are:
cyclooctadienepalladium chloride, cyclooctadienepalladium iodide, 1,5-hexadienepalladium chloride, 1,5-hexadienepalladium iodide, bis(dibenzylideneacetone)palladium, bis(benzonitrile)palladium(II) chloride, bis(benzonitrile)palladium(II) bromide, bis(benzonitrile)palladium(II) iodide, bis(allyl)palladium, bis(methallyl)palladium, allylpalladium chloride dimer, methallylpalladium chloride dimer, tetramethylethylenediaminepalladium dichloride,
tetramethylethylenediaminepalladium dibromide,
tetramethylethylenediaminepalladium diiodide,
(tetramethylethylenediamine)dimethylpalladium,
cyclooctadieneplatinum chloride, cyclooctadieneplatinum iodide,
1,5-hexadieneplatinum chloride,
1,5-hexadieneplatinum iodide, bis(cyclooctadiene)platinum, potassium ethylenetrichloroplatinate,
cyclooctadienerhodium(I) chloride dimer, norbornadienerhodium(I) chloride dimer,
1,5-hexadienerhodium(I) chloride dimer, tris(triphenylphosphine)rhodium(I) chloride,
hydridocarbonyltris(triphenylphosphine)rhodium(I) chloride,
bis(cyclooctadiene)rhodium(I) perchlorate, bis(cyclooctadiene)rhodium(I) tetrafluoroborate,

bis(cyclooctadiene)rhodium(I) triflate,
bis(acetonitrile)cyclooctadienerhodium(I) perchlorate,
bis(acetonitrile)cyclooctadienerhodium(I) tetrafluoroborate,
bis(acetonitrile)cyclooctadienerhodium(I) triflate,
cyclopentadienerhodium(III) chloride dimer,
pentamethylcyclopentadienerhodium(III) chloride dimer,
(cyclooctadiene)Ru(η^3-allyl)$_2$, ((cyclooctadiene)Ru)$_2$(acetate)$_4$,
((cyclooctadiene)Ru)$_2$(trifluoroacetate)$_4$, $RuCl_2$(arene) dimer,
tris(triphenylphosphine)ruthenium(II) chloride, cyclooctadieneruthenium(II) chloride,
$OsCl_2$(arene) dimer, cyclooctadieneiridium(I) chloride dimer,
bis(cyclooctene)iridium(I) chloride dimer,
bis(cyclooctadiene)nickel, (cyclododecatriene)nickel,
tris(norbornene)nickel,
nickel tetracarbonyl, nickel(II) acetylacetonate,
(arene)copper triflate, (arene)copper perchlorate, (arene)copper trifluoroacetate, cobalt carbonyl.

The complexes based on one or more metals, in particular metals selected from the group consisting of Ru, Co, Rh, Ir, Ni, Pd, Pt, Cu, can be catalysts themselves or can be used for preparing catalysts based on one or more metals, in particular metals selected from the group consisting of Ru, Co, Rh, Ir, Ni, Pd, Pt, Cu. All these complexes are particularly useful in the asymmetric hydrogenation of C=C, C=O or C=N bonds, in which they display high activities and selectivities. In particular, it is found to be advantageous that the ligands of the formula (XIII) can be very well matched in stearic and electronic terms to the respective substrate due to the fact that they can easily be modified over a wide range.

Corresponding catalysts comprise at least one of the complexes of the invention.

Examples:

1. 1,2-bis(α-hydroxyethyl)benzene:
   The preparation of 1,2-bis(α-hydroxyethyl)benzene was carried out by literature methods: Goldschmidt et al., Chem. Ber. 1961, 94, 169.

2. Cyclic sulfate:

The preparation of the cyclic sulfate was carried out by the method of Burk (J. Am. Chem. Soc. 1993, 115, 10125) starting from 1,2-bis(α-hydroxyethyl)benzene.

38 mmol of thionyl chloride in 10 ml of CCl_4 are added dropwise to 31 mmol (5.1 g) of 1,2-bis(α-hydroxyethyl)benzene dissolved in 40 ml of CCl_4 over a period of 30 minutes. After refluxing for 2.5 hours and cooling, the solution is evaporated virtually to dryness. The residue is then taken up in CCl_4, acetonitrile, water (25 ml/25 ml/35 ml) and cooled to 0°C. 0.20 mmol of $RuCl_3 \cdot H_2O$ and 61 mml of $NaIO_4$ are added one after the other to the cold mixture. After a reaction time of one hour, the reaction mixture is diluted with 170 ml of water, extracted four times with 100 ml each time of diethyl ether and the combined ether extracts are washed twice with 60 ml each time of saturated NaCl solution. The extract solution is dried overnight over Na_2SO_4 and subsequently evaporated to a reddish brown serum. Column chromatography using silica gel 60 as stationary phase and n-hexane/ethyl acetate 10:1 as mobile phase gives 1.0 g of pure racemic 1,2-bis(α-hydroxyethyl)benzene cyclosulfate (14% of theory).

As a second method, the procedure of Zhang WO 97/13763 was employed. The yield of pure bis(α-hydroxyethyl)benzene cyclosulfate was 25%, and the ^{1}H-NMR data reported in the literature could be reproduced.

^{1}H-NMR (400, 13 MHz, $CDCl_3$): δ 1.92 (d, 6H, CH_3), 5.56 (q, 2H, CH), 7.35 (m, 2H, CH_{ar}), 7.56 (m, 2H, CH_{ar}) ppm.

3. Isophosphindoline synthesis

(modification of the method of Burk et al., J. Am. Chem. Soc. 1993, 115, 10125)

1.5 mmol of phenylphosphine are dissolved in 35 ml of kethyl-dried THF and admixed with 0.94 ml of 1.6 M n-BuLi solution in n-hexane. After stirring for two hours at room temperature, this solution is added dropwise at –78°C to a mixture of 1.5 mmol (340 mg) of the cyclic sulfate and 20 ml of THF. Four hours after the addition was complete, another 1.09 ml of 1.6 M n-BuLi solution in n-hexane is added dropwise. The solution is slowly warmed to room temperature overnight, and

excess organolithium compound is hydrolyzed using 1 ml of oxygen-free methanol. Complete evaporation of the solution gives a white residue which was firstly examined by means of ^{31}P-NMR as a guide. This crude product contains many by-products in addition to the desired isophosphindoline.

^{31}P NMR (161.99 MHz, $CDCl_3$): δ+21.7 ppm.

GC/MS (70 eV): m/e = 240 (100%, M^+), 225 (25%, M^+-15), 212 (9%), 192 (5%), 178 (6%), 165 (3%), 147 (16%), 131 (17%), 120 (10%), 115 (14%), 109 (12%), 91 (27%), 77 (32%), 65 (2%), 51 (2%), 39 (2%).

4. Purification of the isophosphindoline by oxidation/reduction

The crude isophosphindoline product is oxidized for the purposes of purification and separation of the enantiomers.

The crude product is dissolved in THF and stirred overnight at 20°C in the presence of air, the solution is shaken with 20 ml of saturated NH_4Cl solution, the aqueous phase is washed three times with 20 ml each time of diethyl ether and the combined organic phases are dried over anhydrous sodium sulfate and evaporated to dryness. The crude product obtained in this way comprises, inter alia, 1,3-dimethyl-2-phenylisophosphindoline oxide. Washing with n-hexane and subsequent separate column chromatography of the filtrate and of the filter residue (silica gel, 1. n-hexane/ethyl acetate 10:4, 2. MeOH) gives various fractions of the oxide having purities of from 70 to 90%.

Analytical data:

MS (70 eV): m/e = 256 (100%, M^+), 241 (5% M^+-15), 228 (5%), 200 (4%), 178 (4%), 165 (2%), 147 (1%), 132 (18%), 131 (19%), 129 (5%), 117 (58%), 115 (19%), 91 (14%), 77 (6%), 65 (2%), 51 (4%), 39 (2%);

^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.18 (dd J_{HH}: 7.1 Hz, J_{PH}: 16.7 Hz, 3H, CH_3), 1.55 (dd J_{HH}: 7.6 Hz, J_{PH}: 14.8 Hz, 3H, CH_3), 3.28, 3.30 (2 x m, 1H, CH), 3.54, 3.59 (2 x m, 1H, CH), 7.18-7.41 (m, 9H, CH_{ar}) ppm.

^{31}P NMR (161.99 MHz, C_6D_6): δ +60.4 ppm.

Reduction

0.2 mmol (52 mg) of 1,3-dimethyl-2-phenylisophosphindoline oxide are, without additional solvent, heated with 0.13 mmol of freshly distilled phenylsilane for two hours at 90°C under a protective argon

atmosphere. The reaction mixture is cooled and then extracted with 3 × 2 ml of absolute, oxygen-free diethyl ether and filtered. The filtrate is evaporated and the 1,3-dimethyl-2-phenylisophosphindoline is isolated in a purity of about 80%. Phosphorus-free by-products which have not been identified up to now were not able to be separated off.

^{1}H NMR (400.13 MHz, C_6D_6: δ 1.14 (dd J_{HH}: 7.3 Hz, J_{PH}: 11.2 Hz, 3H, CH_3), 1.49 (dd J_{HH}: 7.7 Hz, J_{PH}: 14.8 Hz, 3H, CH_3), 3.34, 3.40 (2 x m, 1H, CH), 3.50, 3.62 (2 x m, 1H, CH), 6.72....7.39 (m, 9H, CH_{ar}) ppm; ^{31}P NMR (161.99 MHz, $CDCl_3$): δ +21.5 ppm.

5. Resolution of racemic 1,3-dimethyl-2-phenylisophosphindoline 2-oxide
The analytical separation of an ethanolic solution of the racemate of 1,3-dimethyl-2-phenylisophosphindoline 2-oxide is carried out by HPLC (CHIRALCEL OD-H, n-hexane/EtOH 97:3, flow rate: 0.8 ml/min). The retention times are 13.5 min and 20.0 min.
For the preparative separation of the enantiomers of the isophosphindoline oxide and for removing the by-products, a silica gel precolumn was installed and multiple injection into the above-described analytical HPLC column and combination of a total of 75 fractions of each of the two enantiomers gave 5.3 mg of the enantiomer which eluted first and 6.2 mg of the enantiomerically pure isophosphindoline oxide which eluted second. The optical rotation of the two enantiomers could not be determined precisely.

Complexes of 1,3-dimethyl-2-phenylisophosphindoline

6. cis-bis(1,3-dimethyl-2-phenylisophosphindoline)dichloropalladium
0.07 mmol (17 mg) of 1,3-dimethyl-2-phenylisophosphindoline dissolved in 0.3 ml of absolute THF is combined with 0.035 mmol of $[PdCl_2(PhCH)_2]$ dissolved in 0.6 ml of absolute THF under a protective argon atmosphere, the mixture is stirred briefly, filtered through a Pasteur pipette filled with silica gel and evaporated completely. The orange residue is analyzed. This is the cis complex of the formula $PdCl_2$(isophosphindoline)$_2$.

Analytical data:

MS (electron impact ionization (70 eV)): m/e = 586 (2%, PdP_2^+), 584 (2%, PdP_2- $2H^+$), 317 (3%), 240 (100%, M^+), 225 (28%, M^+-15), 212 (3%), 192 (10%), 178 (14%), 165 (7%), 147 (24%), 131 (34%), 129 (10%), 115 (46%), 109 (12%), 91 (59%), 77 (32%), 65 (2%), 51 (2%), 39 (2%)

^{31}P NMR (161.99 MHz, C_6D_6/THF): δ +74.04 ppm.

7. cis-Bis(1,3-dimethyl-2-phenylisophosphindoline)cyclooctadienerhodium tetrafluoroborate

0.05 mmol of $[Rh(COD)_2]BF_4$ is slurried in 1.5 ml of THF and, under a protective argon atmosphere, 0.1 mmol (24 mg) of 1,3-dimethyl-2-phenylisophosphindoline dissolved in 0.1 ml of C_6D_6 is added thereto. After being allowed to stand for about one hour at room temperature, the rhodium COD complex dissolves to form the phospholine complex. The compound is present as a rapidly exchanging diastereomer mixture of the formulae Rh(COD)(R-Isophos)(S-Isophos) and Rh(COD)(R-Isophos)(R-Isophos) or Rh(COD)(S-Isophos)(S-Isophos).

^{31}P NMR (161.99 MHz, C_6D_6): δ +62.3 ppm (broad signal).

8. (1,3-Dimethyl-2-phenylisophosphindoline)cyclooctadienechlororhodium

0.025 mmol of $[Rh(COD)Cl_2]$ is slurried in 1.0 ml of THF and, under a protective argon atmosphere, 0.05 mmol (12 mg) of 1,3-dimethyl-2-phenylisophosphindoline dissolved in 0.1 ml of C_6D_6 is added thereto. After stirring for about 30 minutes at room temperature, the rhodium-COD-Cl complex dissolves to form the isophosphindoline complex.

^{31}P NMR (161.99 MHz, C_6D_6): δ +61.8 ppm (d, J_{PRh} = 154 Hz).

Claims:

1. A complex of the formula (XIV)

$$[M_xP_mL_nS_q]Y_r \qquad (XIV)$$

where

M is a metal center,

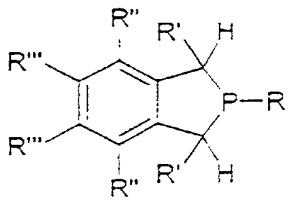
P are organic ligands,

L are identical or different organic or inorganic ligands,

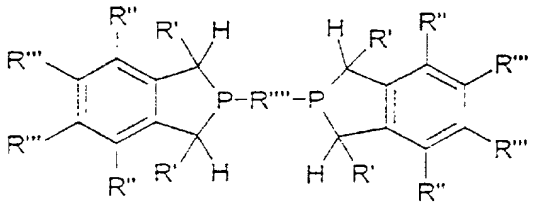
S are coordinating solvent molecules and

Y are noncoordinating anionic equivalents

and x and m are integers greater than or equal to 1, n, q and r are integers greater than or equal to 0, in which one or more identical or different isophosphindolines of the type (VII) or (XIII)



(VII)



(XIII)

are present as ligands P.

2. A complex as claimed in claim 1, wherein the sum m + n + q is less than or equal to 6x.

3. A complex as claimed in claim 1 or 2 in which less than four metal centers, preferably one or two metal centers, are present.

4. A complex as claimed in any of the preceding claims, wherein the metal center or centers M_x comprise at least one transition metal, in particular palladium, platinum, rhodium, ruthenium, osmium, iridium, cobalt, nickel or/and copper.

5. A complex as claimed in any of the preceding claims, wherein, in the formula (VII),

R is hydrogen or an alkyl, aryl, haloaryl or haloalkyl group,

R' are alkyl, aryl, haloaryl or haloalkyl groups,

R" and R"' are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl or haloaryl, alkoxy, amino, dialkylamino or sulfonate groups or fluorine and two adjacent radicals R"/R", R"/R"' or R"'/R"' may also be bridged,

and, in the formula (XIII)

R' are alkyl, aryl, haloaryl or haloalkyl groups,

R" and R"' are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl or haloaryl, alkoxy, amino, dialkylamino or sulfonate groups or fluorine and two adjacent radicals R"/R", R"/R"' or R"'/R"' may also be bridged, and

R"" is an alkanediyl, arenediyl or heteroarenediyl group, where the term alkyl or haloalkyl group encompasses the corresponding cyclo compounds.

6. A complex as claimed in any of the preceding claims, wherein the alkyl, aryl, haloalkyl, haloalkyl, alkoxy or/and dialkylamino groups each have, independently of one another, from 1 to 20, preferably from 1 to 6, carbon atoms.

7. A complex as claimed in any of the preceding claims, wherein the haloalkyl or/and haloaryl groups are CF_3, CH_2CF_3, C_2F_5.

8. A complex as claimed in any of the preceding claims, wherein the alkanediyl, arenediyl or heteroarenediyl group R"" has from 2 to 20 carbon atoms, preferably 2, 3, 4, 5 or 6 carbon atoms, in particular 2 or 6 carbon atoms.

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9. A complex as claimed in any of the preceding claims, wherein the alkanediyl, arenediyl or heteroarenediyl group R"" is ethane-1,2-diyl, benzene-1,2-diyl or furan-3,4-diyl.

10. A complex as claimed in any of the preceding claims, wherein R is phenyl, R' is methyl or ethyl, R" and R"' are hydrogen, methyl or/and phenylene, R"" is benzene-1,2-diyl.

11. A complex as claimed in any of the preceding claims in which chiral ligands P are present.

12. A complex as claimed in any of the preceding claims, wherein a ligand P is an isophosphindoline of the formula (VII) which has two asymmetric centers having the same absolute configuration in positions 1 and 3.

13. A complex as claimed in any of claims 1 to 11, wherein a ligand P is an isophosphindoline of the formula (XIII) which has three or four asymmetric centers having the same absolute configuration in positions 1, 1', 3 and 3'.

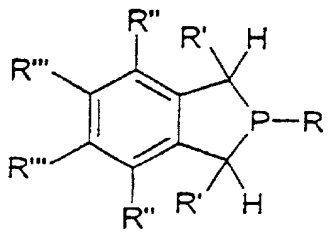
14. A complex as claimed in any of the preceding claims, wherein R is phenyl, R' is methyl, R" and R"' are hydrogen and R"" is benzene-1,2-diyl.

15. A complex as claimed in any of the preceding claims which is enriched in one enantiomer.

16. The use of a complex as claimed in any of claims 1 to 15 as catalyst for asymmetric reactions or polymerizations, in particular for asymmetric hydrogenations, transfer hydrogenations, rearrangements, cyclopropanations, Heck reactions.

Abstract

The invention relates to complexes containing substituted isophosphindolines of the formula (VII) or (XIII)



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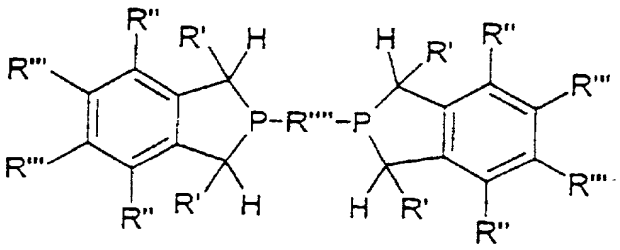

(XIII)

where, in the formula (VII),
R is hydrogen or an alkyl, aryl, haloaryl or haloalkyl group,
R' are alkyl, aryl, haloaryl or haloalkyl groups,
R'' and R''' are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl or haloaryl, alkoxy, amino, dialkylamino or sulfonate groups or fluorine and two adjacent radicals R''/R'', R''/R''' or R'''/R''' may also be bridged,
and, in the formula (XIII)
R' are alkyl, aryl, haloaryl or haloalkyl groups,
R'' and R''' are each, independently of one another, hydrogen, alkyl, aryl, haloalkyl or haloaryl, alkoxy, amino, dialkylamino or sulfonate groups or fluorine and two adjacent radicals R''/R'', R''/R''' or R'''/R''' may also be bridged, and
R'''' is an alkanediyl, arenediyl or heteroarenediyl group, where the term alkyl or haloalkyl group encompasses the corresponding cyclo compounds.

The invention further relates to the use of such complexes as catalysts.

COMBINED DECLARATION AND POWER OF ATTORNEY	Attorney Docket No. 198at29 (8602*32)

As a below named inventor, I hereby declare that:
My residence, post office address and citizenship are as stated below next to my name.
I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled

SUBSTITUTED ISOPHOSPHINDOLINES AND THEIR USE

the specification of which
(check one) ☐ is attached hereto.

☒ was filed on September 23, 1999 as International Patent Application PCT/EP99/07084

was amended on _____ (if applicable)

was amended through _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under 35 U.S.C. §119(a)-(d) or 365(b) of any foreign application(s) for patent or inventor's certificate, or §365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed
198 46 559.9 (Number)	Germany (Country)	October 9, 1998 (Day/Month/Year Filed)	☒ Yes ☐ No
_____ (Number)	_____ (Country)	_____ (Day/Month/Year Filed)	☐ Yes ☐ No

I hereby claim the benefit under 35 U.S.C. §119(e) of any United States provisional application(s) listed below.

_____ (Application No.) _____ (filing date)

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose to the Office all information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

PCT/EP99/07084 (Application Serial No.)	September 23, 1999 (Filing Date)	Published (WO 00/21971) (Status)
_____ (Application Serial No.)	_____ (Filing Date)	_____ (Status) (patented, pending, abandoned)

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

POWER OF ATTORNEY: As a named inventor, I hereby appoint the following attorney(s) and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith:

In the matter of the above-identified application, please recognize Rudolf E. Hutz, Reg. No. 22,397; John D. Fairchild, Reg. No. 19,756; Harold Pezzner, Reg. No. 22,112; Richard M. Beck, Reg. No. 22,580; Paul E. Crawford, Reg. No. 24,397; Patricia Smink Rogowski, Reg. No. 33,791; Robert G. McMorrow, Jr., Reg. No. 30,962; Ashley I. Pezzner, Reg. No. 35,646; William E. McShane, Reg. No. 32,707; Mary W. Bourke, Reg. No. 30,982; Gerard M. O'Rourke, Reg. No. 39,794; James M. Olsen, Reg. No. 40,408; Francis DiGiovanni, Reg. No. 37,310; Eric J. Evain, Reg. No. 42,517; Daniel C. Mulveny, Reg. No. 45,897; and Elliot C. Mendelson (Agent), Reg. No. 42,878, all of P.O. Box 2207, Wilmington, Delaware 19899-2207 as attorneys with full power of substitution to prosecute this application and conduct all business in the Patent and Trademark Office connected therewith..

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FULL NAME OF FOURTH JOINT INVENTOR IF ANY	INVENTOR'S SIGNATURE	DATE
Matthias Beller	Ma Beller	05/21/2001
RESIDENCE		CITIZENSHIP
Bernsteinweg 16, 18119 Rostock, Germany DEX		Germany
POST OFFICE ADDRESS		
Same as above		
FULL NAME OF FIFTH JOINT INVENTOR IF ANY	INVENTOR'S SIGNATURE	DATE
Boris E. Bosch	Boris E. Bosch	05/25/01
RESIDENCE		CITIZENSHIP
Unter Kahlenhausen 42, 50668 Köln, Germany DEX		Germany
POST OFFICE ADDRESS		
Same as above		
FULL NAME OF SIXTH JOINT INVENTOR IF ANY	INVENTOR'S SIGNATURE	DATE
Henrik Junge	Henrik Junge	06/01/01
RESIDENCE		CITIZENSHIP
Albert-Schweitzer-Str. 8, 18147 Rostock, Germany DEX		Germany
POST OFFICE ADDRESS		
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